PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

VENAFORCE FORTE

COMPLEMENTARY MEDICINE

Western Herbal Medicines

This unregistered medicine has not been evaluated by the South African Health Products Regulatory Authority for its quality, safety or intended use.

SCHEDULING STATUS

S0

1 NAME OF THE MEDICINE

A.VOGEL VENAFORCE FORTE (gastro-resistant tablets)
Aesculus hippocastanum L.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gastro-resistant tablet contains:
Aesculus hippocastanum L. (Horsechestnut) *(S3).....157,5 – 225,0 mg
[Fresh seeds, 4 - 6:1 extract corresponding to 50 mg triterpene glycosides, calculated as anhydrous B-aescin providing dry plant equivalent: 0,8 - 1,2 g of herbal drug per tablet]

Sugar free.

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Biconvex, oval-shaped, yellowish-beige coated gastro-resistant tablet.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

A.VOGEL VENAFORCE FORTE is a western herbal remedy used for the treatment and relief of symptoms of chronic venous insufficiency and varicose veins.

Indicated for the following consequences of venous insufficiency:
- tired, heavy, aching & painful legs
- swollen legs
- restless legs
- cramping and sensation of tension in the legs
- unsightly veins

4.2 Posology and method of administration

Posology
Adults over 18 years:
Take 1 tablet 2 times daily.

Special populations
Elderly population:
No dosage adjustment is required for this population.

Paediatric population:
This product is not indicated in patients younger than 18 years.

Method of administration
For oral use only.
Take tablets with meals.
Tablets should be swallowed whole.

Duration of use
At least 4 weeks of treatment may be required before a beneficial effect is observed. Long-term use is possible in consultation with a doctor.

4.3 Contraindications

- A.VOGEL VENAFORCE FORTE should not be used in patients who have a hypersensitivity to the active substance, *Aesculus hippocastanum* L. (Horsechestnut), or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

- If there is inflammation of the skin, thrombophlebitis or subcutaneous induration, severe pain, ulcers, sudden swelling of one or both legs, cardiac or renal insufficiency, a doctor should be consulted immediately as this may be a sign of serious disease.
- A.VOGEL VENAFORCE FORTE contains soya polysaccharides. Patients who are allergic to peanut or soya, should not use A.VOGEL VENAFORCE FORTE.
- If severe symptoms persist for more than 7 days or symptoms worsen during the use of A.VOGEL VENAFORCE FORTE, a doctor, pharmacist or other healthcare professional should be consulted.

Paediatric population
- A.VOGEL VENAFORCE FORTE is not recommended for use in children under 18 years of age.

4.5 Interaction with other medicines and other forms of interaction

None known.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential/Contraception in males and females
No information available.

Pregnancy
No information available.
The safety of this product during pregnancy has not been established. In the absence of sufficient data, the use of A.VOGEL VENAFORCE FORTE during pregnancy is not recommended.

Breastfeeding
No information available.
The safety of this product during breastfeeding has not been established. In the absence of sufficient data, the use of A.VOGEL VENAFORCE FORTE during breastfeeding is not recommended.

Fertility
Fertility studies have not been performed.

4.7 Effects on ability to drive and use machines

A.VOGEL VENAFORCE FORTE has no known effect on mental and/or physical ability to perform or execute tasks or activities requiring mental alertness, judgment and/or sound coordination and vision.

It is not always possible to predict to what extent A.VOGEL VENAFORCE FORTE may interfere with the daily activities of a patient. Patients should ensure that they do not engage in the above activities until they are aware of the measure to which A.VOGEL VENAFORCE FORTE affects them.

4.8 Undesirable effects

It is known that uncoated aescin-preparations can cause gastric symptoms. These symptoms may be avoided by taking the medication during meals and using a film-coated form of administration (A.VOGEL VENAFORCE FORTE is a film-coated, gastro-resistant tablet).

Adverse reactions are grouped into the following frequency classifications: Very common (≥ 1/10), common (≥ 1/100 to < 1/10), uncommon (≥ 1/1 000 to < 1/100), rare (≥ 1/10 000 to < 1/1 000), very rare (< 1/10 000), not known (cannot be assessed from the available data).

Tabulated list of adverse reactions

Body System	Frequency	Undesirable effect
Nervous system disorders	Uncommon	Dizziness (vertigo) and headache
Gastrointestinal disorders	Uncommon	Gastrointestinal complaints (nausea, vomiting, diarrhoea, abdominal pain or discomfort).
Hypersensitivity reactions	Rare	Dermatitis / allergy (pruritus, rash, erythema, eczema).

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reaction Reporting Form**", found online under SAHPRA's publications:
https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose
No case of overdose has been reported.
In overdose, side effects can be precipitated and/or be of increased severity (see section 4.8).

Treatment of overdose should be symptomatic and supportive.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties
Western Herbal Medicine D33.6
Pharmacotherapeutic group and ATC code:
Other capillary stabilizing agents / C05CX03

The exact mechanism of action is not known, but preclinical and clinical pharmacological studies indicate that an effect on venous tone and capillary filtration rate is involved.

Several *in vitro*- and *in vivo*-studies have demonstrated that the antiexudative, antioedematous and venotonic activity of aescin is based on the reduction of the increased activity of lysosomal enzymes in pathological conditions of the vein walls by the prevention of the enzyme-emergence out of the cells. By this effect, a breakdown of the glycocalyx (mucopolysaccharides) in the vessel wall of capillaries and smaller veins is inhibited. The stabilization of the labile lysosomal cell membrane is maintained and the permeability of smaller protein particles into the tissues is controlled.

Based on a systematic review (meta-analysis) of 17 clinical trials, it can be concluded that horsechestnut seed extract (standardised on aescin) significantly reduces symptoms of chronic venous insufficiency, such as oedema, pain and itching compared to placebo.

Level of evidence (according to WHO): Ia (evidence obtained from meta-analysis of randomized controlled trials).

Grade of recommendation (according to WHO): A

5.2 Pharmacokinetic properties
Available data on pharmacokinetic parameters for aescin are of restricted validity and not considered relevant for the dosing regimen of the herbal preparation.

Limited information is available from human studies. In animals the gastrointestinal absorption half-life is about 1 hour. The absolute bioavailability after oral administration is not more than 1 %. In plasma more than 80 % of aescin binds to plasma proteins. Metabolites due to the extensive first-pass-effect of unbound aescin are chemically not identified but pharmacologically inert. The elimination half-life in men is between 15 h and 25 h. After animal studies 2/3rds of the unchanged aescin is excreted via the bile and 1/3rd is eliminated via the urine.

5.3 Preclinical safety data
Available preclinical data indicate low toxicity following oral administration of the herbal preparation.

An *in vitro* study has shown the extract used in A.VOGEL VENAFORCE FORTE to be non-mutagenic. Tests on reproductive toxicity and carcinogenicity have not been performed.

Acute toxicity
Aescin has been tested for acute toxicity in various animal models (mouse, rat, guinea-pig, rabbit, dog). The no effect-dose-limit is about eight times higher than the dose recommended for human treatment. The LD_{50} of orally applied horsechestnut extracts per kg body weight in tested animal species (mouse, rat, rabbit, dog) is about 100 - 250 times higher than the recommended dose in men.

Repeated dose toxicity
Animal experiments have provided no evidence of cumulative toxic activity by oral administrations in two species (rats and dogs) of doses about 50 times higher than the recommended human dosages for up to 34 weeks.

Embryotoxicity, Teratogenicity
Neither embryotoxic nor teratogenic effects have been observed in animal experiments. No relating reports to these effects are documented from children of women who were treated with aescin during pregnancy in a few published studies.

Anaphylaxis
In guinea-pigs daily intraperitoneal injections for 1 week did not induce anaphylactic reactions by an intravenous re-injection after 3 weeks.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients
For the tablet:
Colloidal silica, anhydrous
Copovidone
Maize starch
Microcrystalline cellulose
Soya polysaccharide

For the film coating:
Methacrylic acid - ethyl acrylate copolymer (1:1) dispersion 30 %
Methacrylic acid - methyl methacrylate copolymer (1:1)
Talc
Triethyl citrate

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
60 months unopened.
Use within 3 months of opening.

6.4 Special precautions for storage
No special storage conditions.
Store at or below 25 °C in a cool, dry place.
Store in the original package/container.

6.5 Nature and contents of container
Amber glass bottle (type III glass) with aluminium pilfer proof closure fitted with a polyethylene liner.

Pack size: 30 tablets

6.6 Special precautions for disposal of a used medicine or waste materials derived from such medicine and other handling of the product
No special requirements.

7 THE HOLDER OF THE CERTIFICATE OF REGISTRATION

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8 REGISTRATION NUMBER(S)/REFERENCE NUMBER

Listing number: 029659

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

To be allocated.

10 DATE OF REVISION OF TEXT

August 2021